C. REMARKS

Claims 1-5 and 9-27 have been cancelled without prejudice. Applicants reserve the right to prosecute such claims in a divisional application.

Claim 6 has been amended in order to place the application in better form. The fact that Claim 6 has been amended is not to be construed as an admission by Applicants or Applicants' attorneys that Claim 6, prior to the amendment thereof, was not patentable.

Claims 6-8 stand rejected under 35 U.S.C. 102(b) as being anticipated by Diukman, et al.

Claims 6-8 stand rejected under 35 U.S.C. 102(b) as being anticipated by Barnes, et al.

These rejections are respectfully traversed.

The present invention, as defined broadly in Claim 6, is directed to a method of engrafting mesenchymal stem cells. The method comprises administering isolated mesenchymal stem cells to a fetus in utero.

Diukman discloses the administration of bone marrow containing hematopoietic stem cells to a fetus in utero while Barnes discloses the administration of human whole blood to rabbit and monkey fetuses in utero.

Neither Diukman nor Barnes, however, discloses or even remotely suggests to one of ordinary skill in the art the administration of isolated mesenchymal stem cells to a fetus in utero. Therefore, neither Diukman nor Barnes anticipates Applicants' method as claimed, nor do Diukman and Barnes, taken alone or in combination, render Applicants' method as claimed obvious to one of ordinary skill in the art. It is therefore respectfully requested that the rejections under 35 U.S.C. 102(b) be reconsidered and withdrawn.

Claims 6-8 stand rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a well asserted utility or a well established utility. This rejection is respectfully traversed.

The Examiner has taken the position that practicing the method of the present invention has neither specific nor substantial utility because the implanted mesenchymal stem cells do not act as reservoirs in degenerative diseases as asserted by the specification.

The Examiner, in the Office Action, has admitted that Applicants have reduced to practice the in utero transplantation of mesenchymal stem cells, and that mesenchymal stem cells implanted in utero will distribute into various tissues and organs in a fetus and be detectable in the born animal. Once Applicants demonstrated that the mesenchymal stem cells implanted into various tissues and proliferated into several cell types, one skilled in the art would expect reasonably that such mesenchymal stem cells could be administered to a fetus in order to provide normal stem cells to replace defective cells as they become damaged in degenerative diseases with progressive cellular and organ damage.

The Examiner also has taken the position that there is no objective evidence that the implanted cells will obviate any specific damage that is present or will counteract any potential damage in diseases such as muscular dystrophy, osteoporosis, osteogenesis imperfecta, or collagen disorders. As a specific case in point, the Examiner states that, if an altered form of collagen is expressed by the cells of the host animal, it is unclear how providing a second source of collagen would alleviate any of the consequences of the altered collagen.

Applicants assert that the method of the present invention will provide to a fetus normal mesenchymal stem cells, which can differentiate into, for example, normal muscle cells, normal bone cells, and cells which express normal collagen. One skilled in the art would understand

readily that, for example, normal muscle cells could form normal muscle tissue to counteract the effects of muscular dystrophy, normal bone cells could form normal bone tissue to counteract the effects of osteoporosis or osteogenesis imperfecta, and cells that express normal collagen could counteract the effects of collagen disorders. Therefore, once Applicants demonstrated that mesenchymal stem cells could be engrafted into a fetus and had proliferated into several cell types, one skilled in that art would expect that such mesenchymal stem cells could be used to generate normal cells of various cell types in order to treat a variety of diseases or disorders associated with abnormal cells. Thus, Applicants have shown that the present invention has a well established utility. It is therefore respectfully requested that the rejection under 35 U.S.C. 101 be reconsidered and withdrawn.

Claims 6-8 stand rejected under 35 U.S.C. 112, first paragraph, in that one skilled in the art clearly would not know how to use the claimed invention. This rejection is respectfully traversed.

The Examiner has taken the position that the specification fails to teach any specific or substantial circumstance to practice the method as claimed to provide a reservoir of stem cells or any other of the proposed utilities, in a fetus or born animal.

In support of his position, the Examiner cites the Mackenzie paper, which, at Page 405, states that further investigation is required for specific applications with respect to stem cells that have been implanted in utero.

The mere fact that Mackenzie states that further investigation is needed does not mean that one skilled in the art would not expect reasonably that mesenchymal stem cells could be implanted into a fetus to treat various diseases and disorders.

In fact, at Page 404, Mackenzie describes the transplantation of human mesenchymal stem cells into sheep fetuses in an animal model. Mackenzie states that the results have been very encouraging, and that 28 out of 29 animals tested showed evidence of engraftment by PCR. In addition, Mackenzie notes that immunohistochemistry has shown that, as a result of the implantation of the human mesenchymal stem cells, human cells have been found in cartilage, fat, skeletal and cardiac muscle, lung, thymus, spleen, and brain. Mackenzie also states that in two animals, mesenchymal stem cells persisted for over 13 months, even when transplanted into immunocompetent fetuses.

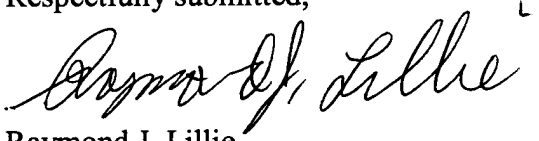
Furthermore, Mackenzie found that the mesenchymal stem cells had differentiated in thymic epithelial cells, bone marrow stromal cells, skeletal muscle cells, and cardiomyocytes.

Based on the results reported by Mackenzie, Mackenzie, in the paragraph bridging Pages 404 and 405, states that such results warrant further testing of the capacity to differentiate along multiple lineages following systemic transplantation. When taken in the entire context of the Mackenzie paper, Mackenzie makes such a statement because Mackenzie has a reasonable expectation that different populations of mesenchymal stem cells can be implanted into fetuses in utero, whereby such mesenchymal stem cells then would differentiate into various cell types in sufficient amounts, and persist in the born animal for a sufficient amount of time in order to treat or counteract the effects of various diseases or disorders. Based on Applicants' disclosure and the Mackenzie paper, one skilled in the art would have a reasonable expectation that one could, without undue experimentation, administer mesenchymal stem cells to a fetus, and such mesenchymal stem cells would differentiate into various cell types, thereby treating or counteracting the effects of various diseases and disorders. For the above reasons and others, the

specification provides an enabling disclosure, and it is therefore respectfully requested that the rejection under 35 U.S.C. 112, first paragraph, be reconsidered and withdrawn.

For the above reasons and others, this application is in condition for allowance, and it is therefore respectfully requested that the rejections be reconsidered and withdrawn and a favorable action is hereby solicited.

Respectfully submitted,



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